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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/745,243	12/21/2000	Narendra Parikh	JBP514	8350

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EXAMINER	
HOLT, ANDRIAE M	

ART UNIT	PAPER NUMBER
1616	

MAIL DATE	DELIVERY MODE
08/30/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/745,243	PARIKH ET AL.	
	Examiner	Art Unit	
	ANDRIAE M. HOLT	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *2-6,8,9,11,13,14,16-19,21,22,24,31-33,35,36 and 73-79* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *2-6,8,9,11,13,14,16-19,21,22,24,31-33,35,36 and 73-79* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to Applicant's amendment filed June 7, 2011. Claims 2-6, 8-9, 11, 13-14, 16-19, 21-22, 24, 31-33, 35-36, and 73-79 are pending in the application. Claims 8, 31, 73, and 75 have been amended. Claims 77-79 are newly added. Claims 2-6, 8-9, 11, 13-14, 16-19, 21-22, 24, 31-33, 35-36, and 73-79 will presently be examined to the extent they read on the elected subject matter of record.

Status of the Claims

Rejections and/or objections not reiterated from the previous Office Action are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

New Rejection Necessitated by Amendment filed June 7, 2011

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 4-6, 8-9, 11, 13-14, 16-19, 21-22, 24, 31, 33, 35-36, and 73-79 are rejected under 35 U.S.C. 103(a) as being unpatentable over CA 2,068,366 in view of Guley et al. (US 4,309,405), Roche (US 5,075,114), Kanai et al. (US 4,868,183), and Uchida et al. (US 5,215,999).

Applicant's Invention

Applicant claims a textured masked particle comprising a) a core containing an active ingredient, b) a first coating layer comprised of a taste masking agent that substantially covers the core, and c) a second coating layer on the surface of the first coating layer. Applicant claims the taste masking agent is comprised of an insoluble film forming polymer and a non-enteric, water soluble polymer. Applicant claims the second coating layer is comprised of i) a water soluble and/or water swellable film forming polymer; and ii) an anti-grit agent selected from the group consisting of polyethylene oxide, polyethylene glycol, and mixtures thereof. Applicant claims the weight ratio of water soluble and/or water swellable film forming polymer to anti-grit agent in the second coating layer is in the range of about 20:80 to about 80:20.

Determination of the scope of the content of the prior art (MPEP 2141.01)

CA 2,068,366 teaches a taste-masked free-flowing powder including microcapsules having a particle size of 300 μm or less that includes a core element including at least one pharmaceutically active ingredient; a substantially smooth and continuous microcapsule coating on the core element formed from a coating composition including a water insoluble polymer (page 3, lines 1-11). CA 2,068,366

teaches a taste-masking microcapsule powder composition may be in the form of sprinkles, tablets; including chewable tablets and lozenges. CA 2,068,366 teaches the pharmaceutical composition may be provided in the form of dispersible or effervescent tablets (page 8, lines 12-20). CA 2,068,366 teaches the water insoluble polymer may be selected from ethyl cellulose and cellulose acetates (water insoluble polymers) (page 8, lines 26-32). CA2,068,366 teaches in one embodiment the taste-masked microcapsule coating composition may include the coating composition of a water insoluble polymer, one or more enteric polymer (enteric polymer), an acid-soluble (reverse enteric) polymer, and a partially water soluble polymer (water soluble polymer). CA 2,068,366 teaches the enteric polymer is selected from cellulose acetate phthalate, hydroxypropyl methyl cellulose phthalate (HPMCP), polyvinyl acetate phthalate, or hydroxypropyl methylcellulose acetate succinate (specific enteric polymers) (page 9, lines 19-38). CA 2,068,366 teaches when the microcapsule coating is a sustained release coating the coating may include a water insoluble polymer (water insoluble polymer); an enteric polymer (enteric polymer) and a partially water soluble component (water soluble polymer) (page 10, lines 4-12). CA 2,068,366 teaches the partially water-soluble component may be selected from hydroxypropyl methylcellulose, hydroxypropyl cellulose, polyethylene glycol and mixtures thereof (hydroxypropyl methylcellulose and polyethylene glycol) (page 10, lines 13-18). CA 2,068,366 teaches the modified release core coating contains a water insoluble polymer; an acid-soluble (reverse enteric) polymer and a partially water soluble component (page 10, lines 27-35). CA 2,068,366 teaches the modified release may provide substantially no or a slow rate of release at

alkaline pH, but substantially immediate or more rapid release at acid pH (page 10, lines 19-16). CA 2,068,366 teaches the reverse enteric polymer is selected from the acrylate copolymer sold under the trade designation Eudragit E100 or natural polymers such a Chitin (page 11, lines 2-8) (non-enteric water soluble polymer). Eudragit E100 is a cationic copolymer based on dimethylaminoethyl methacrylate and neutral methacrylic ester as evidenced by the EUDRAGIT® E100 specification sheet.

CA 2,068,366 teaches the microcapsule compositions may include carriers or excipients (page 11, lines 23-31). CA 2,068,366 teaches the microcapsule composition can be used with acetaminophen, theophylline, ranitidine hydrochloride, and NSAIDS (page 8, lines 2-8). CA 2,068,366 teaches the method for preparing the microcapsules on page 13, lines 1-23).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

CA 2,068,366 does not teach the second coating layer is comprised of a water soluble and/or water swellable film forming polymer and an anti-grit agent such as polyethylene oxide or polyethylene glycol, the claimed ratios, or that the non-enteric polymer is hydroxypropyl cellulose. It is for this reason Kanai et al., Uchida et al., and Guley et al. are added as secondary references.

Guley et al. teach sustained release compositions comprising a core containing a drug, a seal coating surrounding the core, and an sugar coating surrounding the seal coated core (Abstract). Guley et al. teach the core water soluble polymers are selected from synthetic polymers, such as, hydroxypropyl methylcellulose (col. 2, lines 38-44).

Guley et al. teach the water insoluble polymer mixture is selected from synthetic polymers, such as ethylcellulose (col. 2, lines 45-50). Guley et al. teach the seal coating is selected from film forming materials which is capable of substantially protecting the core during its passage from the stomach to the intestines. Guley et al. teach that the seal coating may be selected from enteric and non-enteric film forming materials and mixtures thereof (col. 3, lines 7-14). Guley et al. teach that a preferred non-enteric seal coating includes a mixture of at least two hydrocolloids, one a water soluble polymer and one a water-insoluble. An example of such a mixture is the use of ethyl cellulose with hydroxypropyl methylcellulose (col. 3, lines 30-46). Guley et al. teach other non-enteric materials useful in the seal coating include hydroxypropyl cellulose (col. 3, lines 47-50). Guley et al. teach that the seal coated, compressed cores are then sugar coated with a sugar coating suspension (col. 3, lines 60-68).

Roche teaches a medicament coating comprising a blend of cellulose acetate and hydroxypropyl cellulose. The coating provides excellent taste masking while still permitting acceptable bioavailability of the active ingredient (col. 2, lines 20-28).

Kanai et al. teach in preparation example 2, compound 1, crystalline cellulose, corn starch and magnesium stearate were ground and formulated into tablets with use of sugar-coated punch having a radius of 8 mm. Kanai et al. teach that the resulting tablets were coated with a film coating agent consisting of hydroxypropyl methyl cellulose (hydroxypropyl methyl cellulose), polyethylene glycol 6000 (polyethylene glycol), castor oil and ethanol, giving film-coated tablets of the composition (col. 39, lines 20-27).

Uchida et al. teach that the N-2-propenyl-4-[(2-ethylphenyl)amino]-8-methoxyquinoline-3-carboxamide hydrochloride compound, AVICEL, corn starch and magnesium stearate were mixed, polished and then tableted by means of a R10mm punch (for sugar-coated tablets). Uchida et al. further teach the tablets thus obtained were coated with a film comprising hydroxypropyl methyl cellulose (hydroxypropyl methyl cellulose), polyethylene glycol-6000 (polyethylene glycol), castor oil and methanol to prepare film-coated tablets (col. 64, lines 1-19).

Finding of prima facie obviousness
Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of invention to use the teachings of CA 2,068,366, Guley et al., Roche, Kanai et al., and Uchida et al. and use a non-enteric polymer, such as hydroxypropyl cellulose, in the formulation. CA 2,068,366 teaches various formulations of active ingredients/agents formulated with a water insoluble polymer to mask taste. The formulations that are taught by CA 2,068,366 include insoluble polymers that form films, enteric polymers, and water soluble polymers that also form films, including hydroxypropyl methylcellulose and hydroxypropyl cellulose. One skilled in the art at the time the invention was made would have been motivated to use a non-enteric polymer such as hydroxypropyl cellulose because the polymers that are the partially water-soluble components taught in CA 2, 068,366 are the same non-enteric polymers disclosed by Guley et al., hydroxypropyl methylcellulose and hydroxypropyl cellulose. In addition, it is known in the pharmaceutical art to combine hydroxypropyl cellulose with ethylcelluose or

cellulose acetate to provide taste masking for pharmaceuticals, as evidenced by the teaching of Roche. Therefore, the skilled artisan would have been motivated to use hydroxypropyl cellulose as a non-enteric polymer in the formulations with a reasonable expectation of success.

It would have been obvious to one of ordinary skill in the art at the time of invention to use the teachings of CA 2,068,366, Guley et al., Roche, Kanai et al., and Uchida et al. and use a water soluble and/or water swellable film forming polymer and an anti-grit agent such as polyethylene oxide or polyethylene glycol as the second layer. CA 2,068,366 teaches various formulations of active ingredients/agents formulated with a water insoluble polymer to mask taste. The formulations that are taught by CA 2,068,366 include insoluble polymers that form films, enteric polymers, and water soluble polymers that also form films. One skilled in the art at the time the invention was made would have been motivated to use a water soluble polymer such as hydroxypropyl methylcellulose and an anti-grit agent such as polyethylene glycol as the second coating because as evidenced by Kanai et al. and Uchida et al. these ingredients are used to prepare film-coated tablets. As such, the skilled artisan would have been motivated to try a film-coating formulation that is well-known in the art, especially when the ingredients of the film-coating formulation can be used to prepare to the active agents with two coatings.

In reference to the claimed ratios of 20:80 to about 80:20, 50:50, and 60:40 to about 40:60. Kanai et al. and Uchida et al. each teach that hydroxypropyl methyl cellulose and polyethylene glycol are mixed at a 3:1 or 66.7:33.3. This ratio would fall

within the range of 20:80 to about 80:20. In addition, absent data showing unexpected results, as noted in the previous office action, the use of the ratio would be a matter of routine experimentation and optimization. Accordingly, this type of modification would have been well within the purview of the skilled artisan and no more than an effort to optimize results.

Therefore, the claimed invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made because every element of the invention has been fairly suggested by the cited reference.

Response to Arguments

Applicant's arguments filed October 6, 2010 have been fully considered but they are not persuasive. Applicant argues that neither Kanai et al. nor Uchida et al. disclose or suggest that a coating of HPMC and polyethylene glycol can be used for particles. In response to Applicant's arguments, as noted in the previous office actions, Kanai et al. and Uchida et al. were used as evidence to teach that a water soluble and/or water swellable film forming polymer and an anti-grit agents such as polyethylene oxide or polyethylene glycol are used as second layers in the preparation of pharmaceutical formulations. The primary reference, CA 2,068,366, teaches active ingredient particles that are coated with two layers, a water insoluble polymer and a water soluble polymer. One skilled in the art at the time the invention was made would have motivated to use a water soluble polymer such as hydroxypropyl methylcellulose and an anti-grit agent such as polyethylene glycol as the second coating in the formulations taught by the primary references because Kanai et al. and Uchida et al. teach these ingredients are

used to prepare film-coated tablets. While, tablets are not particles, the technology of film coating particle or tablets with the same compounds or combinations of compounds is well known and documented in the art, as evidenced by the teachings of Yang et al., from the previous rejection, which teach the use of a mixture of hydroxypropyl methylcellulose and polyethylene glycol as a second coating of particles. As such, the skilled artisan would have been motivated to try a film-coating formulation that is well-known in the art, especially when the ingredients of the film-coating formulation can be used to prepare the coating layers used in the formulations taught by the primary reference, CA 2,068,366.

In response to Applicant's argument that Kanai et al. and Uchida et al. do not disclose or suggest the current claimed methods of manufacturing coated particles, Kanai et al. and Uchida et al. were used as evidence to teach that a water soluble and/or water swellable film-forming polymer and an anti-grit agents such as polyethylene oxide or polyethylene glycol are used as second layers in the preparation of pharmaceutical formulations. The primary reference, CA 2,068,366, teach the method of manufacturing coated particles. CA 2,068,366 teaches the method for preparing the microcapsules on page 13, lines 1-23.

As noted in the previous rejection, in response to Applicant's purported unexpected results, the reported results are not commensurate in scope with Applicant's claims. Applicant claims a texture masked particle comprising a) a core containing an active ingredient, b) a first coating layer comprised of a taste masking agent that substantially covers the core, and c) a second coating layer on the surface of

the first coating layer. Applicant claims the taste masking agent is comprised of an insoluble film forming polymer and a non-enteric, water-soluble polymer. Applicant claims the second coating layer is comprised of i) a water soluble and/or water swellable film forming polymer; and ii) an anti-grit agent selected from the group consisting of polyethylene oxide, polyethylene glycol, and mixtures thereof. Applicant claims the weight ratio of water soluble and/or water swellable film forming polymer to anti-grit agent in the second coating layer is in the range of about 20:80 to about 80:20. The formulation of the instant invention prepared comprises preparation of particles comprising acetaminophen as the active ingredient, ethyl cellulose as the insoluble film forming particle of the first coating, and hydroxypropyl methylcellulose and polyethylene glycol 8000 as the texture masking or second layer. The formulation does not contain a non-enteric, water soluble polymer. Acetaminophen represents a single species of active ingredients, as claimed. Ethylcellulose represents a single species of insoluble film forming polymers. Hydroxypropyl methylcellulose represents a single species of water soluble and/or water swellable film forming polymers. The examiner cannot determine if the purported unexpected results of "less grittiness" provided by the combination of acetaminophen, ethylcellulose, hydroxypropyl methylcellulose and polyethylene glycol 8000 is reflective of the combination of any active ingredient, any water insoluble film-forming polymer, any water soluble film-forming polymer, and any anti-grit agent, known and unknown. In addition, Applicant's independent claims are directed to particles and method of making particles and not chewable tablets, as tested in the examples. Therefore, the examiner notes that the claims are not commensurate

in scope with the examples provided.

None of the claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andriae M. Holt whose telephone number is (571)272-9328. The examiner can normally be reached on 7:00 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Richter Johann can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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